Modeling Alexander disease using patient-specific induced pluripotent stem cells

Grant Award Details

Modeling Alexander disease using patient-specific induced pluripotent stem cells

Grant Type: Basic Biology IV

Grant Number: RB4-06277

Project Objective: The goal of this proposal is to establish an iPSC-based cellular model for Alexander disease (AxD), a severe neurodegenerative disease caused by gene mutations in GFAP, the major intermediate filament protein in astrocytes.

Investigator:

Name:	Yanhong Shi
Institution:	City of Hope, Beckman Research Institute
Type:	PI

Disease Focus: Neurological Disorders, Pediatrics

Award Value: $1,366,656

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE (Year 4)

View Report

Grant Application Details

Application Title: Modeling Alexander disease using patient-specific induced pluripotent stem cells

Public Abstract: Alexander disease (AxD) is a devastating childhood disease that affects neural development and causes mental retardation, seizures and spasticity. The most common form of AxD occurs during the first two years of life and AxD children show delayed mental and physical development, and die by the age of six. AxD occurs in diverse ethnic, racial, and geographic groups and there is no cure; the available treatment only temporally relieves symptoms, but not targets the cause of the disease. Previous studies have shown that specific nervous system cells called astrocytes are abnormal in AxD patients. Astrocytes support both nerve cell growth and function, so the defects in AxD astrocytes are thought to lead to the nervous system defects. We want to generate special cells, called induced pluripotent stem cells (iPSCs) from the skin or blood cells of AxD patients to create an unprecedented, new platform for the study and treatment of AxD. We can grow large quantities of iPSCs in the laboratory and then, using novel methods that we have already established, coax them to develop into AxD astrocytes. We will study these AxD astrocytes to find out how their defects cause the disease, and then use them to validate potential drug targets. In the future, these cells can also be used to screen for new drugs and to test novel treatments. In addition to benefiting AxD children, we expect that our approach and results will benefit the study of other, similar childhood nervous system diseases.

Statement of Benefit to California: It is estimated that California has approximately 12% of all US cases of AxD, a devastating childhood neurological disorder that leads to mental retardation and early death. At present, there is no cure or standard treatment available for AxD. Current treatment is symptomatic only. In addition to the tremendous emotional and physical pain that this disease inflicts on Californian families, it adds a medical and fiscal burden larger than that of any other states. Therefore, there is a real need to understand the underlying mechanisms of this disease in order to develop an effective treatment strategy. Stem cells provide great hope for the treatment of a variety of human diseases. Our proposal to establish a stem cell-based cellular model for AxD could lead to the development of new therapies that will represent great potential not only for Californian health care patients, but also for the Californian pharmaceutical and biotechnology industries. In addition to benefiting the treatment of AxD patients, we expect that our approach and results will benefit the study of other related neurological diseases that occur in California and the US.